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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,962	09/08/2003	Mendy S. MacCabee	49321-102	3139

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EXAMINER
KIM, JENNIFER M

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,962	MACCABEE ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,12 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,12 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 3, 2008 have been received and entered into the application.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 11-12 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "non-aerosol" lack literal support in the specification as originally filed.

This is a New Matter rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 depend from claim 11 which requires topical administration of a **non-aerosol** formulation. However, claim 12 is drawn to administration of sprays, aerosolized or mobilized particles, which is contradictory to claim which it depends from.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8, 11, 12 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biesalski (U.S.Patent No. 5,556,611) of record in view of Belloni (U.S.Patent No. 6,339,107 B1).

Biesalski teaches a pharmaceutical preparation consisting of **retinoic acid** as an active substance suitable for a topical treatment of mucosal disease in man and animal. (abstract). Biesalski teaches the preparation can be formulated in an aerosol formulation. (abstract). Biesalski teaches the effective amount of the active substance is from 0.01-50% by weight. (column 6, line 44). This range encompasses and touches Applicants' amounts set forth in claim 8. Biesalski teaches that the preparation is effective for treating functional impairments in the mucous membranes of humans and animals, in particular in the respiratory epithelium and the epithelia of the nose-throat

cavity. Biesalski teaches that the treatment is also useful in reduced activity of the ciliated epithelium and disturbances of the mucous membranes of the reparatory tract. (column 10, lines 24-45). Biesalski teaches the preparation is effective for treating acute and chronic bronchitis, acute and chronic functional disturbances due to impairment of tracheobronchial epithelium and bronchopulmonary dysplasia.

Biesalski do not expressly teach the non-aerosol, depot formulation of retinoic acid, and the cause of the ciliated epithelial structure damage due to the surgical intervention.

Belloni teaches a composition comprising retinoic acid for the treatment of emphysema including the airspaces distal to the terminal bronchioles and destruction of their walls. (abstract, column 4, lines 50-60). Belloni teaches that topical administration of retinoic acid can be formulated as solutions, gels, ointments, creams, suspension, etc. as are well-known in the art. (column 8, lines 14-17). Belloni teaches that retinoic acid can be formulated for oral liquid preparations such as suspensions, elixirs and solutions, as well as transmucosal and buccal administration. (column 8, lines 35-40, line 40-65, column 9, lines 1-6).

It would have been obvious to one of ordinary skill in the art to modify the aerosol formulation of retinoic acid taught by Biesalski to topical non-aerosol, depot formulations such as solution, ointments and transdermal as taught by Belloni for the treatment of damaged ciliated epithelial structure. One would have been motivated to make such a modification because Belloni teaches that retinoic acid can be formulated for the treatment of damaged respiratory walls and because such damaged respiratory walls

are routinely treated topically with retinoic acid as taught by Belloni et al. in various topical formulations. There is a reasonable expectation of success in treating a damaged ciliated epithelial structure comprising topical administration of non-aerosol such as ointment comprising retinoic acid because such formulation and the method of treating damaged or destruction of respiratory walls are well known in view of Belloni.

It would have been obvious to one of ordinary skill in the art to employ retinoic acid preparation taught by Biesalski as modified by Belloni for the treatment of damaged ciliated epithelial structure regardless of cause because both Biesalski et al. and Belloni teach that the retinoic acid preparation is effective for the treatment of impaired ciliated epithelium and damaged respiratory walls. One would have been motivated to employ the retinoic acid preparation taught by Biesalski as modified by Belloni for a condition of damaged ciliated epithelium or damaged respiratory at any cause including the surgical intervention in order to treat the condition or the symptoms of damaged ciliated epithelium at any cause including the damage from the surgical intervention. There is a reasonable expectation of successfully treating damaged ciliated epithelium because both Biesalski and Belloni teach the effectiveness of the preparation in repairing and treating damaged ciliated epithelium or damaged respiratory walls in man or animal with retinoic acid.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed January 3, 2008 have been fully considered but they are not persuasive. Applicants argue that Applicants have amended independent claims 1 and 11 to recite "comprising topical administration of a **non-aerosol** depot formulation of a therapeutically effective amount of composition comprising vitamin A to a damaged ciliated epithelial structure,.. wherein treating of the damaged ciliated epithelial structure is achieved", and that the support of the amendment is found through out the originally-filed specification, which teaches non-aerosol administration to topical depot formulations (e.g. page 8, line 8 through page 10, line 4; also examples using gel formulation as a topical depot formulation). The instant specification as originally filed has been carefully reviewed and considered. However, it is determined that at the time the application was filed, Applicants' were in possession of the specific drug formulations such as ointments and gel formulations. However, the formulation drawn to "non-aerosol" in general **was not described** in the specification in a such a way as to reasonably convey to one skilled in the relevant art that the Applicants have the possession of the term "non-aerosol" formulation in general at the time the invention was filed. The term "non-aerosol" lack literal support in the specification as originally filed and, therefore, the new matter rejection made in this Office Action is deemed proper. Applicants argue that Biesalski is absolutely silent on surgery-related damage. This is not found persuasive because both references (Biesalski and Belloni) teach that

retinoic acid is effective in destruction or damage to respiratory wall. Therefore, there is a reasonable expectation of successfully treating destruction or damage to respiratory wall of a patient regardless of the cause. Applicants argue that Biesalski fundamentally teaches away from the present depot form of administration. This is not found persuasive because Belloni teaches Applicants' topical "depot" formulation such as ointment comprising retinoic acid are useful for treating damaged respiratory walls. Therefore, Biesalski's selection of aerosol formulation rather than non-aerosol formulation such as an ointment as their formulation based on one set of criteria does not "teach away" from formulating a composition comprising retinoic acid on the another set. Biesalski et al. do not suggest that non-aerosol formulation does not work on retinoic acid composition, but rather that aerosol formulation better suited their (unspecified/specified) need. There remains, even after the Beisalski's aerosol formulation, a reasonable expectation of success that retinoic acid in non-aerosol formulation such as an ointment would work in treatment of damaged respiratory wall, as long as one were willing to use different criteria for selection. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

March 24, 2008